

adenocarcinoma, urinary bladder transitional carcinoma, Hodgkin lymphoma, MALT lymphoma, non-Hodgkins lymphoma (NHL) diffuse large B, NHL, thymoma, lipoma, and liposarcoma.

94. (New) A method of treating an individual suffering from cancer comprising, administering to said individual a Pin1 inhibitor such that treatment occurs.
95. (New) The method of claim 94 wherein the cancer is selected from the group consisting of oligodendroglioma, astrocytoma, glioblastomamultiforme, endometriod carcinoma, endometrium serous carcenoma, uterus carcinosarcoma, thyroid adenocarcinoma, thyroid follicular cancer, thyroid medullary cancer, thyroid papillary carcinoma, parathyroid adenocarcinoma, adrenal gland adenoma, adrenal gland cancer, pheochromocytoma, esophagus adenocarcinoma, hepatocellular carcinoma, mouth cancer, gall bladder adenocarcinoma, pancreatic adenocarcinoma, urinary bladder transitional carcinoma, Hodgkin lymphoma, MALT lymphoma, non-hodgkins lymphoma (NHL) diffuse large B, NHL, thymoma, lipoma, and liposarcoma.

REMARKS

Claims 1-48 were pending in the application. Claims 1-48 have been canceled without prejudice. New claims 49-95 have been added. Accordingly, after the amendments presented herein have been entered, claims 49-95 will remain pending. For the Examiner's convenience all of the pending claims are set forth herein in Appendix A.

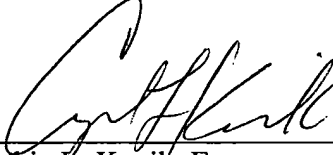
Support for the new claims may be found throughout the specification and claims as originally filed.

No new matter has been added. Any cancellation of the claims should in no way be construed as an acquiescence to any of the Examiner's rejections and was done solely to expedite the prosecution of the application. Applicants reserve the right to pursue the claims as originally filed in this or a separate application(s).

CONCLUSION

In view of the foregoing amendments and foregoing remarks, it is respectfully submitted that the application is in condition for allowance. If a telephone conversation with Applicants' Attorney would expedite the prosecution of the above-identified application, the Examiner is urged to call Applicants' Attorney at (617) 227-7400.

Respectfully submitted,



Cynthia L. Kanik, Esq.
Registration No. 37,320
Attorney for Applicant

LAHIVE & COCKFIELD, LLP
28 State Street
Boston, MA 02109
Tel. (617) 227-7400

Dated: October 8, 2002

Appendix A

49. A method of detecting abnormal cell growth in a test sample isolated from the rectum, mouth, central nervous system, endometrium, head, neck, parotid tissue, brain, gall bladder, esophagus, thyroid, parathyroid, uterus, or adrenal tissue, comprising the steps of
assessing the level of Pin1 in a test sample from a mammal,
wherein an elevation in the levels of Pin1 is indicative of abnormal cell growth in the tissue.
50. The method of claim 49, wherein the level of Pin1 is a protein level.
51. The method of claim 49, wherein the level of Pin1 is a nucleic acid level.
52. The method of claim 49, wherein the test sample is a tissue sample.
53. The method of claim 49, wherein the test sample is a body fluid test sample selected from the group consisting of blood, ascites, serum, urine, saliva, sputum, phlegm, pus, mucus, bone marrow, lymph, tears or brain body fluid test sample.
54. The method of claim 49 wherein, detecting the abnormal cell growth in a mammal, comprises the steps of:
detecting a level of Pin1 in a test sample; and
comparing the level of Pin1 in the test sample with a control level, and wherein a difference in the level of Pin1 in the test sample is indicative of abnormal cell growth in the mammal.
55. The method of claim 49, wherein the abnormal cell growth is cancer.
56. The method of claim 55, wherein the cancer is selected from the group consisting of oligodendroglioma, astrocytoma, glioblastomamultiforme, endometriod

carcinoma, endometrium serous carcenoma, uterus carcinosarcoma, thyroid adenocarcinoma, thyroid follicular cancer, thyroid medullary cancer, thyroid papillary carcinoma, parathyroid adenocarcinoma, adrenal gland adenoma, adrenal gland cancer, pheochromocytoma, esophagus adenocarcinoma, hepatocellular carcinoma, mouth cancer, gall bladder adenocarcinoma, pancreatic adenocarcinoma, urinary bladder transitional carcinoma,, Hodgkin lymphoma, MALT lymphoma, non-Hodgkins lymphoma (NHL) diffuse large B, NHL, thymoma, lipoma, and liposarcoma.

57. A method of claim 50 wherein, the method of detecting the level of Pin1 protein in a test sample from a mammal, comprises the steps of:

contacting the test sample with an antibody having specificity for Pin1 under conditions suitable for binding of the antibody to Pin1 thereby resulting in the formation of a complex between the antibody and Pin1;

detecting the complex between the antibody and Pin1; and

comparing the amount of the complex in the test sample with an amount of a complex in a control sample, wherein an elevation in the amount of the complex between the antibody and Pin1 in the test sample compared to the complex in the control sample is indicative of abnormal cell growth.
58. The method of claim 55, wherein the antibody is a polyclonal antibody.
59. The method of claim 55, wherein the antibody is a monoclonal antibody.
60. The method of claim 55, wherein the antibody is detectably labeled.
61. The method of claim 60, wherein the detectable label is selected from the group consisting of a radioactive, enzymatic, biotinylated and fluorescent label.

62. The method of claim 55, wherein the complex is detected by incubating the complex with a second antibody specific for the complex, wherein the secondary antibody comprises a detectable label.
63. The method of claim 51, wherein the method further comprises the step of performing a polymerase chain reaction with oligonucleotide primers capable of amplifying the Pin1 nucleic acid prior to detection.
64. The method of claim 51, wherein the method further comprises the steps of:
contacting a test sample obtained from the mammal with a nucleic acid probe to a Pin1 nucleic acid;
maintaining the test sample and the nucleic acid probe under conditions suitable for a hybridization;
detecting the hybridization between the test sample and the nucleic acid probe;
and
comparing the hybridization in the test sample from the mammal to a control test sample without the cellular proliferation, wherein an elevation in the hybridization signal in the test sample from the mammal compared to the control sample is indicative of abnormal cell growth.
65. A method of determining the stage of cancer in a test sample isolated from the rectum, mouth, central nervous system, endometrium, head, neck, parotid tissue, brain, gall bladder, esophagus, thyroid, parathyroid, uterus, or adrenal tissue, of a mammal, comprising assessing a level of Pin1 in the test sample, wherein the level of Pin1 correlates with the stage of the cancer.
66. The method of claim 65, wherein the level of Pin1 is a protein level.
67. The method of claim 66, wherein the level of Pin1 is a nucleic acid level.

68. The method of claim 65 wherein, detecting the abnormal cell growth in a mammal, comprises the steps of:
- detecting a level of Pin1 in a test sample; and
- comparing the level of Pin1 in the test sample with a control level, and wherein a difference in the level of Pin1 in the test sample is indicative of abnormal cell growth in the mammal.
69. A method of claim 65 wherein, the method of detecting the level of Pin1 protein in a test sample from a mammal, comprises the steps of:
- contacting the test sample with an antibody having specificity for Pin1 under conditions suitable for binding of the antibody to Pin1 thereby resulting in the formation of a complex between the antibody and Pin1;
- detecting the complex between the antibody and Pin1; and
- comparing the amount of the complex in the test sample with an amount of a complex in a control sample, wherein an elevation in the amount of the complex between the antibody and Pin1 in the test sample compared to the complex in the control sample is indicative of abnormal cell growth.
70. The method of claim 69, wherein the antibody is a polyclonal antibody.
71. The method of claim 69, wherein the antibody is a monoclonal antibody.
72. The method of claim 69, wherein the antibody is detectably labeled.
73. The method of claim 68, wherein the method further comprises the step of performing a polymerase chain reaction with oligonucleotide primers capable of amplifying the Pin1 nucleic acid prior to detection.
74. The method of claim 68, wherein the method further comprises the steps of:

contacting a test sample obtained from the mammal with a nucleic acid probe to a Pin1 nucleic acid;

maintaining the test sample and the nucleic acid probe under conditions suitable for a hybridization;

detecting the hybridization between the test sample and the nucleic acid probe; and

comparing the hybridization in the test sample from the mammal to a control test sample without the cellular proliferation, wherein an elevation in the hybridization signal in the test sample from the mammal compared to the control sample is indicative of abnormal cell growth.

75. The method of claim 68, wherein the cancer is selected from the group consisting of oligodendroglioma, astrocytoma, glioblastomamultiforme, endometriod carcinoma, endometrium serous carcenoma, uterus carcinosarcoma, thyroid adenocarcinoma, thyroid follicular cancer, thyroid medullary cancer, thyroid papillary carcinoma, parathyroid adenocarcinoma, adrenal gland adenoma, adrenal gland cancer, pheochromocytoma, esophagus adenocarcinoma, hepatocellular carcinoma, mouth cancer, gall bladder adenocarcinoma, pancreatic adenocarcinoma, urinary bladder transitional carcinoma, Hodgkin lymphoma, MALT lymphoma, non-Hodgkins lymphoma (NHL) diffuse large B, NHL, thymoma, lipoma, and liposarcoma.
76. A method of claim 68 wherein the stage of cancer is determined by assessing a level of a Pin1 nucleic acid in a test sample, comprising the steps of:

performing a polymerase chain reaction with oligonucleotide primers capable of amplifying the Pin1 nucleic acid;

detecting a level of amplified nucleic acid fragments of the Pin1 nucleic acid; and

comparing the level of amplified nucleic acid fragments in the test sample to a sample comprising varying stages of the abnormal cell growth, wherein the stage of abnormal cell growth in the mammal is determined.
77. A method of claim 55 wherein the stage of cancer is determined by assessing a level of a Pin1 nucleic acid in a test sample, comprising the steps of:

contacting a test sample obtained from the mammal with a nucleic acid probe to a Pin1 nucleic acid;

maintaining the test sample and the nucleic acid probe under conditions suitable for hybridization of the probe to Pin1 nucleic in the sample;

detecting the hybridization between the Pin1 nucleic acid of the test sample and the nucleic acid probe; and

comparing the hybridization in the test sample from the mammal to hybridization of the nucleic probe to Pin1 in a control, wherein the control sample comprises varying stages of the abnormal cell growth, thereby determining the stage of the abnormal cell growth in the mammal.

78. A method of evaluating the efficacy of a treatment of abnormal cell growth in the rectum, mouth, central nervous system, uterine cervix, endometrium, head, neck, parotid tissue, brain, gall bladder, esophagus, lung, thyroid, parathyroid, uterus, or adrenal tissue of a mammal, comprising the step of
- comparing a level of Pin1 in at least two test samples, wherein the test samples comprise a first test sample obtained at a first time and a second test sample obtained at a later second time,
- wherein a decrease in the level of Pin1 between the two test samples indicates the efficacy of the treatment of the abnormal cell growth in the mammal.
79. The method of claim 78, wherein the level of Pin1 is a protein level.
80. The method of claim 78, wherein the level of Pin1 is a nucleic acid level.
81. The method of claim 78, wherein detecting the abnormal cell growth in a mammal, comprises the steps of:
- detecting a level of Pin1 in a test sample; and
- comparing the level of Pin1 in the test sample with a control level, and wherein a difference in the level of Pin1 in the test sample is indicative of abnormal cell growth in the mammal.

82. A method of claim 78 wherein, the method of detecting the level of Pin1 protein in a test sample isolated from the rectum, mouth, central nervous system, endometrium, head, neck, parotid tissue, brain, gall bladder, esophagus, thyroid, parathyroid, uterus, or adrenal tissue, from a mammal, comprises the steps of:
- contacting the test sample with an antibody having specificity for Pin1 under conditions suitable for binding of the antibody to Pin1 thereby resulting in the formation of a complex between the antibody and Pin1;
- detecting the complex between the antibody and Pin1; and
- comparing the amount of the complex in the test sample with an amount of a complex in a control sample, wherein an elevation in the amount of the complex between the antibody and Pin1 in the test sample compared to the complex in the control sample is indicative of abnormal cell growth.
83. The method of claim 78, wherein the antibody is a polyclonal antibody.
84. The method of claim 78, wherein the antibody is a monoclonal antibody.
85. The method of claim 78, wherein the antibody is detectably labeled.
86. The method of claim 78, wherein the method further comprises the step of performing a polymerase chain reaction with oligonucleotide primers capable of amplifying the Pin1 nucleic acid prior to detection.
87. The method of claim 78, wherein the method further comprises the steps of:
- contacting a test sample obtained from the mammal with a nucleic acid probe to a Pin1 nucleic acid;
- maintaining the test sample and the nucleic acid probe under conditions suitable for a hybridization;

detecting the hybridization between the test sample and the nucleic acid probe;
and

comparing the hybridization in the test sample from the mammal to a control test sample without the cellular proliferation, wherein an elevation in the hybridization signal in the test sample from the mammal compared to the control sample is indicative of abnormal cell growth.

88. A kit for determining the level of Pin1 in a test sample isolated from the rectum, mouth, central nervous system, endometrium, head, neck, parotid tissue, brain, gall bladder, esophagus, thyroid, parathyroid, uterus, or adrenal tissue of a mammal comprising one or more reagents for detecting Pin1.
89. The Kit of claim 88, wherein one of the reagents is an antibody.
90. The kit of claim 89, wherein one of the reagents is a DNA probe.
91. The kit of claim 90, wherein one of the reagents is a control.
92. A method for determining whether a subject having cancer of the rectum, mouth, central nervous system, endometrium, head, neck, parotid tissue, brain, gall bladder, esophagus, thyroid, parathyroid, uterus, or adrenal tissue, is likely to respond to treatment comprising a Pin1 inhibitor compound, the method comprising:
 - assessing the level of Pin1 in a test sample from the subject; and
 - comparing the level of Pin1 in the test sample to the level of Pin1 in normal tissue, whereby an increased level of Pin1 in the test sample is indicative that the subject is likely to respond to treatment comprising a Pin1 inhibitor compound.
93. The method of claim 92 wherein the cancer is selected from the group consisting of oligodendroglioma, astrocytoma, glioblastoma multiforme, endometrial carcinoma, endometrium serous carcinoma, uterus carcinosarcoma, thyroid

adenocarcinoma, thyroid follicular cancer, thyroid medullary cancer, thyroid papillary carcinoma, parathyroid adenocarcinoma, adrenal gland adenoma, adrenal gland cancer, pheochromocytoma, esophagus adenocarcinoma, hepatocellular carcinoma, mouth cancer, gall bladder adenocarcinoma, pancreatic adenocarcinoma, urinary bladder transitional carcinoma, Hodgkin lymphoma, MALT lymphoma, non-Hodgkins lymphoma (NHL) diffuse large B, NHL, thymoma, lipoma, and liposarcoma.

94. A method of treating an individual suffering from cancer comprising, administering to said individual a Pin1 inhibitor such that treatment occurs.
95. The method of claim 94 wherein the cancer is selected from the group consisting of oligodendroglioma, astrocytoma, glioblastomamultiforme, endometriod carcinoma, endometrium serous carcenoma, uterus carcinosarcoma, thyroid adenocarcinoma, thyroid follicular cancer, thyroid medullary cancer, thyroid papillary carcinoma, parathyroid adenocarcinoma, adrenal gland adenoma, adrenal gland cancer, pheochromocytoma, esophagus adenocarcinoma, hepatocellular carcinoma, mouth cancer, gall bladder adenocarcinoma, pancreatic adenocarcinoma, urinary bladder transitional carcinoma, Hodgkin lymphoma, MALT lymphoma, non-hodgkins lymphoma (NHL) diffuse large B, NHL, thymoma, lipoma, and liposarcoma.